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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,971	08/09/2000	Thomas William Rademacher	1012-100US	5898

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/601,971	RADEMACHER ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 15-20* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

The **examiner** of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Group Art Unit 1644, Technology Center 1600

1. Applicant's amendment, filed 04/23/03 (Paper No. 15), is acknowledged.

Claims 1-9 and 15-20 are pending.

Claims 8-9 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1-7 and 15-20, read on the elected species of specific antagonist wherein specific antagonist is an inhibitor of enzyme GPI-PLD and specific cell type is mast cells and under consideration in the instant application.

2. It is noted that the title of the invention disclosed on page 1 of the current specification is not the same as the title of the invention disclosed on the Amendments, filed on 08/09/00, 07/29/02 and 04/23/03 (Paper NOs: 3, 11and 15).

3. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on 03/29/2000. It is noted, however, that applicant has not filed a certified copy of the GB99/00981 application as required by 35 U.S.C. 119(b).

In view of the amendment, filed 04/23/03 (Paper No. 15,) the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to an IPG antagonist, wherein said antagonist is : (a) an antibody capable of specifically binding to IPGs, or (b) an antibody capable of specifically binding GPI-PLD does not reasonably provide enablement for: (i) a method for inhibiting

release of an IPG from mast cells, the method comprising exposing the mast cell to *any* IPG antagonist, as claimed in claim 16; or (ii) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to any IPG antagonist *in vitro* or *in vivo* , as claimed in claims 17 and 18-19 respectively; or (iii) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to *an* IPG antagonist, wherein the IPG antagonist comprises :(a) any substance capable of inhibiting or preventing IPG release in mast cells, or (b) any inhibitor of the enzyme GPI-PLD, or (c) any competitive antagonist of the IPGs release, as claimed in claim 20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Applicant's arguments, filed 04/23/03 (Paper No. 15), have been fully considered, but have not been found convincing.

Applicant asserts that the specification provides guidance and examples for determining whether an IPG antagonist, e.g. an inhibitor of GPI-PLD, inhibits the release of IPG from mast cells , examples of IPG antagonist, such as antibodies and the guidance of how to produce said antibodies.

Contrary to Applicant's assertion the issue raised is not the ability of one skill in the art to make antibody , but that the claims as written encompass the genus of IPG antagonist. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences.

Applicant discloses a limited number of specific IPG antagonist, such as an antibody capable of specifically binding to IPGs, or ((a) an antibody capable of specifically binding to IPGs, or (b) an antibody capable of specifically binding GPI-PLD (see page 6, lines 1-20 in particular) that can be used in a method for inhibiting release of an IPG from mast cells. Applicant has not taught how to make and/or use a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to *any* IPG antagonist, as claimed in claim 16; or (ii) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to any IPG antagonist *in vitro* or *in vivo* , as claimed in claims 17 and 18-19 respectively; or (iii) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to *an* IPG antagonist, wherein the IPG antagonist comprises :(a) any substance capable of inhibiting or preventing IPG release in mast cells, or (b) any inhibitor of the enzyme GPI-PLD, or (c)any competitive antagonist of the IPGs release, as claimed in claim 20. The structural and functional characteristics of said IPG antagonist are not defined in the claim.

Protein chemistry is probably one of the most unpredictable areas of biotechnology . It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. Colman *et al.,* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Moreover, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Moreover, Applicant himself acknowledge that the action of IPG antagonist is tissue specific(see page 6, line 21 in particular).
The specification fails to provide sufficient guidance as to which core structure of *any* IPG antagonist is essential for maintain their inhibitory activity and which changes can be made in their structure and still maintained the same function.

Applicant is relying upon certain biological activities and the disclosure of a limited species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies *any* IPG antagonist, or *an* IPG antagonist, wherein the IPG antagonist comprises :(a) any substance capable of inhibiting or preventing IPG release in mast cells, or (b) any inhibitor of the enzyme GPI-PLD, or (c) any competitive antagonist of the IPGs release. Therefore, structurally unrelated *any* IPG antagonist, or *an* IPG antagonist, wherein the IPG antagonist comprises : (a) any substance capable of inhibiting or preventing IPG release in mast cells, or (b) any inhibitor of the enzyme GPI-PLD, or (c) any competitive antagonist of the IPGs release encompassed by the claimed invention other than "an antibody capable of specifically binding to IPGs, or (b) an antibody capable of specifically binding GPI-PLD; " would be expected to have greater differences in their activities.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use (i) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to *any* IPG antagonist, as claimed in claim 16; or (ii) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to any IPG antagonist *in vitro* or *in vivo* , as claimed in claims 17 and 18-19 respectively; or (iii) a method for inhibiting release of an IPG from mast cells, the method comprising exposing the mast cell to *an* IPG antagonist, wherein the IPG antagonist comprises :(a) any substance capable of inhibiting or

preventing IPG release in mast cells, or (b) any inhibitor of the enzyme GPI-PLD, or (c)any competitive antagonist of the IPGs release, as claimed in claim 20 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 and 15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al. (US. Patent NO. 5,418,147) for the same reasons set forth in the previous Office Action, Paper No: 13 mailed 10/21/02.

Applicant's arguments, filed 04/23/03 (Paper No. 15), have been fully considered, but have not been found convincing.

Applicant asserts that amended the claim 1 recites "wherein the IPG antagonist acts specifically on mast cells" - the functional limitation that is not found in patent'147.

Contrary to Applicant's assertion, the Patent '147 teaches a method of making a composition comprising IPG antagonist that is a substance which is capable of inhibiting release of the IPG by inhibiting the enzyme GPI-PLD. The reference composition comprises the antibody against GPI-PLD in a pharmaceutically acceptable excipient. (see columns 15 –17 in particular). Although the reference is silent about composition acting specifically on mast cells, this functional limitation would be inherent properties of the referenced composition because said composition comprising the same antibody against GPI-PLD as claimed. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not acts specifically on mast cells as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teaching anticipates the claimed invention.

6. No claim allowed

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. For example, on page 1, line 9 the word "inositolphosphoglycan" is misspelled. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
June 9, 2003

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